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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/794,851	02/04/97	BARANY	F 19603/461(CR

HM12/1108

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EXAMINER	
RICIGLIANO, J	
ART UNIT	**PAPER NUMBER**
1618	24

DATE MAILED: 11/08/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/794,851	Barany et al.
Examiner	**Group Art Unit**
Joseph W. Ricigliano Ph. D.	1618

☒ Responsive to communication(s) filed on *Aug 25, 1999* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-43, 45-80, 82-88, and 138-148* is/are pending in the application.

Of the above, claim(s) *67-74* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-43, 45-66, 75-80, 82-88, and 138-148* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. This action is responsive to the amendment of 8/25/99 (paper number 20).

2. Claims 1-148 were pending in the instant application, claims 89-137 were previously canceled, and claim 148 added by the amendment of 3/1/99. Claims 44 and 81 were canceled by the amendment of 8/25/99.

3. Claims 1-43, 45-80 and 82-88 and 138-148 are pending in the instant application. Claims 67-74 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1-43, 45-66, 75-80, 82-88 and 138-148 are currently being examined on their merits.

New Grounds of Rejection

Claim Objections

4. Claims 58 and 59 are objected to because of the following informalities concerning the language inserted by amendment.

Claim 58 has been amended to recite "wherein the genetic disease has a known nucleotide sequence," however, genetic diseases do not have technically "have" known nucleotide sequences, rather they correlates with known nucleotide sequences. Altering the recitation to recite "wherein the genetic disease correlates with a known nucleotide sequence" or the use of similar language would be preferable

Claim 59 has similarly been amended to recite the detection of cancer having a known nucleotide sequence. As cancers do not "have a known nucleotide sequence" but rather correlate with the presence of known nucleotide sequences or oncogenic sequences a change in the claim

language to recite to detect a cancer which correlates with the presence of a known nucleotide sequence or oncogeny" or the use of similar language would be preferable.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 1-5, 11-21 and 24-43, 45-66, 75-77,79, 80, 83, 87, 88 and 138-148 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiedmann et al (1994) in view of, Barany (PCR Methods and Applications, 1991a) Zaun et al [US 5, 415, 839], Guo et al (1994) and Reddy [US 5,648,213]

See the teachings of Wiedmann et al (1994) in view of, Barany (PCR Methods and Applications, 1991a) Zaun et al [US 5, 415, 839] and Guo et al (1994) as applied to claims 1-5, 11-21 and 24-43, 45-66, 75-77,79, 80, 83, 87, 88 and 138-148 under 35 U.S.C. 103(a) as being in the office action of 12/16/97, paper number 7 and the office action of 11/10/98, paper number 17.

The claims as amended on 3/1/99 (paper number 20) required that the first probe have an oligonucleotide target-specific portion and an oligonucleotide addressable array specific portion which were distinct from each other. The rejection of the claims as being unpatentable over Wiedmann et al (1994) in view of, Barany (PCR Methods and Applications, 1991a) Zaun et al (US 5, 415, 839), Guo et al (1994) was previously withdrawn specifically because this limitation

was not met or fairly suggested by the Wiedmann, Barany, Zaun and Guo references as combined (see paragraph 9 of the office action of 6/8/99, paper number 21).

However, Reddy et al teach the use of oligonucleotide pairs in detecting analytes. Reddy specifically teach that it is advantageous to substitute double stranded oligonucleotide pairs for antibody-antigen pairs when conducting assays in which one member of the pair is attached to the analyte and the other is attached support. Upon contacting under hybridization conditions the double stranded complex forms and the oligonucleotide analyte conjugate is removed from solution by being specifically bound to the corresponding support bound member of the oligonucleotide pair (See the abstract and column 1 lines 1-62).

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made to substitute an oligonucleotide pair for the antibody antigen capture pair utilized in the references as combined because Reddy et al teach using hybridizable oligo-nucleotide pairs for the capture of analytes on a solid phase support. One of ordinary skill in the art would have been motivated to do so because Reddy teaches the advantages of using oligonucleotide capture reagents in the detection of analytes including the ability to reuse the oligonucleotide labeled supports. One of ordinary skill would reasonably have expected to be successful because Reddy had previously utilized oligonucleotides to capture oligonucleotide labeled analytes.

7. Claims 6-10, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiedmann et al (1994) in view of, Barany (PCR Methods and Applications, 1991a) Zaun et al

[US 5, 415, 839], Guo et al (1994) and Reddy [US 5,648,213] as applied to claims 1-5, 11-21 and 24-43, 45-66, 75-77,79, 80, 83, 87, 88 and 138-148 *supra* in further view Telenti et al.

See the teaching of Wiedmann et al (1994) in view of, Barany (PCR Methods and Applications, 1991a) Zaun et al [US 5, 415, 839], Guo et al (1994) and Reddy [US 5,648,213] *supra.*

The references as combined above fail to teach the quantitation of nucleotide amplification reaction products by providing a known amount of a nucleotide sequence as an internal standard.

Telenti et al.(1992) teach that PCR, another nucleotide amplification reaction, can be quantitated by providing a known amount of an internal standard sequence (abstract, page 259).

It would have been *prima facia* obvious at the time the invention was made to one of ordinary skill in the art to combine the use of an internal standard as a quantitation method as taught by Telenti et al. for the quantitation of PCR products with the ligase amplification reaction as taught by the references as combined *supra*, because Telenti et al. taught the use of internal standards (or "competitive strands" as they are sometimes called by others) for quantitation of nucleic acid amplification products. One of ordinary skill in the art would have been motivated to do so to obtain a direct assessment of the amount of target present in their assay samples and to be able to normalize the sample results for quantitative comparison.

8. Claims 78, 82, 84-86 are rejected under 35 U.S.C. 103(a) as being unpatentable Wiedmann et al (1994) in view of, Barany (PCR Methods and Applications, 1991a) Zaun et al [US 5, 415, 839)], Guo et al (1994) and Reddy [5,648,213] as applied to claims 1-5, 11-21 and

24-43, 45-66, 75-77,79, 80, 83, 87, 88 under 35 U.S.C. 103(a) *supra* and further in view of Sambrook et al.

See the teaching of Wiedmann et al (1994) in view of, Barany (PCR Methods and Applications, 1991a) Zaun et al [US 5, 415, 839], Guo et al (1994) and Reddy [US 5,648,213] *supra.*

The references as combined above fail to teach methods of hybridization the stripping of blots (oligonucleotide arrays) for reuse or the use of exonuclease.

Sambrook et al. teach hybridization of Southern-blots using oligonucleotide probes and the use of nucleotides (sheared and denatured salmon sperm DNA) between target oligonucleotides to which probes do not bind with specificity (pages 9.47-9.55). Sambrook also teaches the cleaning (or stripping) of Southern blots (page (9.58) and the use of exonuclease (see page 5.78-5.79 and 5.84-5.85).

It would have been prima facia obvious at the time the time the invention was made to one of ordinary skill in the art to employ: the conditions for hybridizing oligonucleotide probes to immobilized nucleotides (e.g., Southern-blots etc) including barrier oligonucleotides and exonuclease in the stripping of blots as taught by Sambrook et al. with the LDR methods as taught by the references combined *supra*, because Sambrook et al. had taught Southern blot techniques and the use of exonuclease to digest DNA. One of ordinary skill in the art would have been motivated to use these methodologies in order to obtain clear specific hybridization of nucleotide probes to immobilized target nucleotides with a low background and to be able to

reuse the immobilized array of nucleotides (as taught by the Reddy reference) which can be difficult, time consuming and expensive to prepare.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph W. Ricigliano Ph. D. whose telephone number is (703) 308-9346. The examiner can be reached on Monday through Thursday from 7:00 A.M. to 5:30 P.M.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

10. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Donald E. Adams Ph. D., can be reached at (703) 308-0570.

Joseph W. Ricigliano Ph. D.

KEITH D. MacMILLAN
PRIMARY EXAMINER